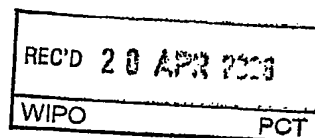


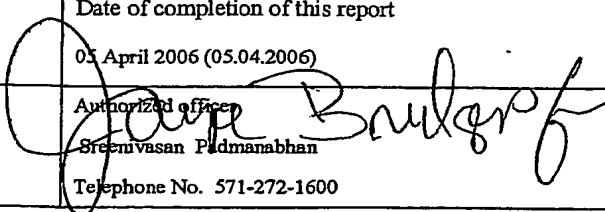
PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference PCT 21309Y	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US03/40561	International filing date (day/month/year) 19 December 2003 (19.12.2003)	Priority date (day/month/year) 23 December 2002 (23.12.2002)
International Patent Classification (IPC) or national classification and IPC IPC: A61K 31/34(2006.01) USPC: 514/461		
Applicant MERCK FROSST CANADA & CO.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>7</u> sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of <u> </u> sheets.</p>		
<p>3. This report contains indications relating to the following items:</p> <p>I <input checked="" type="checkbox"/> Basis of the report</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input type="checkbox"/> Non-establishment of report with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand 09 June 2004 (09.06.2004)	Date of completion of this report 05 April 2006 (05.04.2006)	
Name and mailing address of the IPEA/US Mail Stop PCT, Attn: IPEA/ US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Authorized officer  Sreenivasan Padmanabhan Telephone No. 571-272-1600	

Form PCT/IPEA/409 (cover sheet)(July 1998)

USSN 10/539,872

EXHIBIT 2

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US03/40561

I. Basis of the report**1. With regard to the elements of the international application:***

- ☒ the international application as originally filed.
- ☒ the description:
pages 1-17 as originally filed
pages NONE filed with the demand
pages NONE filed with the letter of _____
- ☒ the claims:
pages 18-20 as originally filed
pages NONE as amended (together with any statement) under Article 19
pages NONE filed with the demand
pages NONE filed with the letter of _____
- ☐ the drawings:
pages NONE as originally filed
pages NONE filed with the demand
pages NONE filed with the letter of _____
- ☐ the sequence listing part of the description:
pages NONE as originally filed
pages NONE filed with the demand
pages NONE filed with the letter of _____

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language _____ which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing

- ☐ contained in the international application in printed form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages NONE
- ☐ the claims, Nos. NONE
- ☐ the drawings, sheets/fig NONE

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).**

* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

** Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US03/40561**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement****1. STATEMENT**

Novelty (N)	Claims 1-20	YES
	Claims NONE	NO
Inventive Step (IS)	Claims NONE	YES
	Claims 1-20	NO
Industrial Applicability (IA)	Claims 1-20	YES
	Claims NONE	NO

2. CITATIONS AND EXPLANATIONS

Claims 1-20 meet the criteria set out in PCT Article 33(2), because the prior art does not teach a method of treating Parkinson's disease in a human in need of such treatment comprising: the administration to a human in need of such treatment of an antiparkinson therapeutic amount of an antiparkinson agent and an anti-inflammatory effective amount of a selective COX-2 inhibitor.

Claims 1-20 lack an inventive step under PCT Article 33(3) as being obvious over TEISMANN et al.

TEISMANN et al. teach that inflammatory responses seen in Parkinson's disease brains are contribute to the pathogenesis of Parkinson's disease. TEISMANN et al. teach that inhibition of COX-1 and COX-2 seems to be neuroprotective in the MPTP-mouse model.

TEISMANN et al. conclude that COX-2 inhibition may be a suitable therapeutic strategy in the treatment of Parkinson's disease.

TEISMANN et al. do not teach the actual treatment of Parkinson's disease with the combination of a selective COX-2 inhibitor and antiparkinson agent.

It would have been obvious to one of ordinary skill in the art to employ the combination of COX-2 inhibitors and antiparkinson agent in a human for the treatment of Parkinson's disease because TEISMANN et al. teach that COX-2 inhibitors are effective as neuroprotective agent in MPTP-mouse model and may be suitable for the therapeutic strategy in the treatment of Parkinson's disease. Moreover, one of ordinary skill in the art would be motivated to combine COX-2 inhibitor and antiparkinson agent in a single treatment in order to achieve at least an additive effect.

Claims 1-20 meet the criteria set out in PCT Article 33(4) because a method of treating Parkinson's disease in a human in need of such treatment comprising: the administration to a human in need of such treatment of an antiparkinson therapeutic amount of an antiparkinson agent and an anti-inflammatory effective amount of a selective COX-2 inhibitor has an industrial applicability in pharmaceutical art.